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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,107	11/03/2003	Steven P. Schwendeman	22727/04196	5145

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	**PAPER NUMBER**
1618	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,107	SCHWENDEMAN ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time, amendment and remarks, all filed 12/04/2006. Claim 1 is currently amended. Claims 1-7 are pending.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

The as filed specification does not support a PLGA biodegradable polymeric delivery system that has a level of from 10% to 30% w/w pore forming agent/polymer. Original claim provides support for level of 10% to 40% w/w.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cleland et al. (US 5,643,605).

Cleland discloses compositions and methods for encapsulating adjuvants or biologically active agents in microsphere compositions (abstract, column 1, lines 8-10 and column 3, lines 1-9). The composition comprises PLGA microspheres encapsulating adjuvants (column 3, lines 18-20). The ratio of lactide to glycolide is from 100:0 to 0-100 weight percent (column 3, lines 22-23 and claim 1). The microspheres have a median diameter of 20-100μm (column 3, lines 25-27); adjuvants, which are biologically active agents, are released in a triphasic pattern (column 3, lines 44-52); and the viscosity of the PLGA polymers is 0.1 to 1.2 dL/g (column 3, lines 40 and 58). Cleland further teaches a method for encapsulating the adjuvants in the PLGA microspheres. The method comprises dissolving PLGA in an organic solvent to produce a solution, adding adjuvant to the solution to produce PLGA-adjuvant mixture, adding the mixture to an emulsification bath to produce microspheres comprising second emulsion and hardening the microspheres to produce hardened microspheres comprising encapsulated adjuvants (column 3, line 64 to column 4 line 8). The formulation further comprises carriers and the carriers used in the prior art are those described in Remington's Pharmaceutical Sciences, 16th edition, 1980, (column 7, lines 4-10). Specifically, Cleland teaches that the formulation comprises preservatives, buffer or buffers, polyethylene glycol, mannitol and poloxamer non-ionic surfactant (column 9, lines 24-34). The pH of the formulation ranges from about 5-8 (column 9, lines 35-40). Cleland discloses proteins as adjuvants (column 9, lines 59-67). Cleland teaches that various molecular weights and lactide to glycolide ratios of PLGA used. The molecular weight of the PLGA ranges from 12 kDa to 100 kDa and that ratio of lactide to glycolide ranges from 50:50 to 75:25 (column 10, lines 2-5).

The polyethylene glycols and the poloxamer surfactants of the prior art are referenced as known and available on the market and therefore, have known molecular weights. But since the molecular weights recited in the application do not have units, a comparison of molecular weights cannot be made. It is thus assumed that the molecular weight of polyethylene glycols and poloxamer of the prior art is comparable to the claimed molecular weights. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Cleland. One having ordinary skill in the art would have been motivated to prepare the PLGA composition of Cleland according to the method taught in Cleland. Although Cleland is silent on the molecular weight of the polyethylene glycols and poloxamer, one having ordinary skill in the art would know to use polyethylene glycol and poloxamer of specified molecular since the polyethylene glycol and poloxamer are known and marketed (column 9, lines 25-30). In the absence of a showing the recited molecular weights of polyethylene glycol and poloxamer are not critical over the prior art.

Response to Arguments

3. Applicant's arguments filed 12/04/06 have been fully considered but they are not persuasive.

Applicant argues that Cleland's method involves a first step of dissolving PLGA in an organic solvent to provide a solution, ii) adding aqueous adjuvant solution to the organic solution, iii) adding the resulting solution from i) and ii) to an emulsification bath to produce microspheres. "Any PEG or poloxamer in Cleland" if used, is added to the aqueous adjuvant solution to protect the adjuvant from the organic solvent; that the amount of PEG and/or

poloxamer in Cleland is 0.1% to 30% (w/v) based on antigen solution vs. applicant's 10% to 30% (w/w) based on polymer.

Response:

Regarding process steps outlined in i), ii) and iii) and the use of the PEG or Poloxamer in Cleland vs. applicant's purpose:

While applicant insists that the sequence of adding the ingredients makes the PEG and/or poloxamer to act as pore forming agents as the microsphere degrades, it is noted that pore forming ability is characteristic/properties of the PEG and/or the poloxamer. Properties or characteristic of a chemical or compound is inert to that chemical or compound, and in this case PEG or poloxamer, and not to the sequence of adding the chemical to form a composition. PEG is a known pore-forming agent (see claim 13 of US 4,795,644 to Zentner). Thus, although Cleland does not disclose that the PEG or Poloxamer is used as pore former, it is noted that the pore forming ability of the PEG or Poloxamer flows from the art recognized properties of these polymers. Therefore, if the PEG or poloxamer is acting as a pore forming agent in applicants' invention, then the same PEG or poloxamer would also act as a pore former in the prior art even if the art has not described the PEG or poloxamer as such. PEG or Poloxamer as pore forming agent as recited by applicants, or PEG/Poloxamer as stabilizer for protein as in the prior art, are functions of the PEG or Poloxamer flowing from the property of the PEG or Poloxamer. Also, one of the steps in the instant invention is a lyophilization step, which is one of the steps of drying disclosed by Cleland.

10-30% (w/w) in claimed invention vs. 0.1-30% (w/w)

Applicant's reference that Cleland uses 0.1-30% PEG with respect to the adjuvant/antigen volume while the claimed invention uses 10-30% PEG (w/w) with respect to the polymer in the claimed invention is noted. However, Cleland's disclosure in column 9, lines 33 and 34 regarding the 0.1-30% (w/v) appears to be directed to non-ionic surfactants (column 9, lines 28-34) and not to PEG and/or trehalose. Specifically, column 9, lines 13-23, says that "the mass ratio of trehalose to polypeptide, which is antigen or adjuvant (column 6, lines 21-31), is about 1000:1 to 1:1000 with 100:1 to 1:100 preferred and 1:1 to 1:10, most preferred; the mass ratio of PEG to polypeptide is about 100:1 to 1:100 with 1:1 to 1:10 preferred; that the preferred ratio is chosen on the basis of excipient concentration that permits maximum solubility of polypeptide with minimum denaturation of the polypeptide. During encapsulation, ½ mL of the adjuvant solution at 200 mg/mL, i.e. 100 mg of adjuvant, is used with 3 g of the PLGA (column 13, lines 53-55; column 14, lines 12-14). The mass ratio thus ranges from (100 X 100 mg trehalose): 3 g adjuvant (76% w/w) to (1 X 100 mg Trehalose): 3g adjuvant (3% w//w); for PEG it ranges from (100 x 100 mg): 3g adjuvant (76%) to (1 x 100 mg PEG): 3 g adjuvant (3%). There is thus at least a point(s) within the range of 76% to 3% that touché(s) the recited range of 10% to 30%. The recitation of a range in the claims indicates that no one specific ratio provides unexpected and unusual results and applicant' statement in the remarks is not unexpected since the Cleland reference discloses points within the recited range. Since the amount of PEG in Cleland with respect to the polypeptide (adjuvant) ranges from 76% to 3%, the recited range is encompassed in the Cleland range and is rendered obvious by Cleland. Thus the 10% to 30% allows for ratios within the Cleland range of 3% to 76%.

pH

Therefore, since both the composition of the claimed invention and the prior art contain PEG or Poloxamer and biological agent, and mass ratio of PEG to adjuvant that overlap, it is reasonable to expect that the pH of the microenvironment would be the same for formulations that undergo lyophilization or vacuum drying, during which volatile excipients are expelled at the appropriate temperature and pressure. A pH of 5-8 in the prior art as described above is greater than 3, which is the pH called for by the claims.

No claim is allowed.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER